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gREVIEW

STATE-OF-THE-ART REVIEW

Tobacco Cessation Approaches and Impact on CVD

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Tobacco smoking is a major risk factor for atherosclerotic vascular diseases including cardiovascular, cerebrovascular, and peripheral arterial diseases, and aortic aneurysms. Secondhand smoke and smokeless tobacco confers an increased risk for cardiovascular disease (CVD).

Cessation of smoking is found to be the most effective secondary prevention strategy in controlling CVD, including stroke. Smoking cessation is associated with significant reduction in deaths due to arrhythmia. It improves the lipid profile of patients. The benefits of smoking cessation are seen in post-coronary artery bypass graft patients and in patients undergoing surgery for abdominal aortic aneurysms.

Smoking cessation exhibits a biphasic impact on the cardiovascular system, with an early improvement in the vasoactive properties of blood vessels and a late response on the pathology of atherosclerosis spanning several years.

Among the different tobacco cessation strategies available, psychosocial and behavioral interventions are primary and apparently easy to implement. Because the long-term success of these strategies is low, most guidelines recommend adding pharmacotherapy to the counseling methods. Pharmacotherapy includes nicotine replacement therapies, drugs such as bupropion and nicotine receptor partial agonists such as varenicline. Overall, various smoking cessation strategies result in low long-term quit rates (<30%) in patients with CVD.

However, tobacco cessation strategies are often not given adequate importance in the clinical practice by physicians treating patients with CVD. Further research is needed to improve compliance both to behavioral and pharmacotherapies to enhance quit rates.

Tobacco smoking is a major risk factor for atherosclerotic vascular diseases including cardiovascular, cerebrovascular, and peripheral arterial diseases and aortic aneurysms [1]. Compared with never smokers, the risk of myocardial infarction is increased 3-fold in men and 6-fold in women who smoke more than 20 cigarettes in a day [1,2]. Smoking accounted for 36% of population-attributable risk of a first myocardial infarction (MI) in the INTERHEART (A Study of Risk Factors for First Myocardial Infarction in 52 Countries and Over 27,000 Subjects) study [3]. In addition, involuntary smoking (secondhand smoke [SHS]) has been found to increase the risk of CVD by 25–30%, as indicated in the 2006 U.S. Surgeon General's report [4].

Cessation of smoking may be as effective or more than other secondary prevention strategies in CVD [5]. Despite all available evidence, tobacco cessation strategies are often not given adequate importance in the clinical practice by physicians treating patients with CVD.

This review discusses the impact of tobacco cessation on CVD and the various approaches at the individual level to tackle this problem. In the initial sections, we deal with the observational evidence of the impact of smoking cessation in primary and secondary prevention settings and in the control of CVD risk factors. Subsequently, we deal with the different tobacco cessation strategies available and the impact of each modality. The last section deals with the problems associated with each strategy and the possible solutions. We also have included a small section on the strategies in the pipeline on smoking cessation at the end of this paper.

IMPACT OF TOBACCO CESSATION ON CVD

The positive effect of smoking cessation on *primary prevention* of cardiovascular events was demon-

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GLOBAL HEART, VOL. 7, NO. 2, 2012
July 2012: 129–138

strated in the British Regional Heart Study, which examined changes in cardiovascular risk factors and incidence of MI in a cohort of 7,735 middle-aged men observed prospectively over a period of 25 years, from 1978 to 2003. There was a 62% reduction in the hazard of MI over this period, of which cessation of smoking itself could account for a 23% reduction and was the highest contributor in this regard [6].

Smoking cessation remains the single most important *secondary prevention strategy* in smokers with CVD to date. Smoking increases the risk of all-cause mortality and cardiovascular deaths in both male and female smokers of any type of tobacco, irrespective of the frequency of smoking (Table 1) [7]. The rates of both cardiovascular mortality and nonfatal reinfarctions are significantly reduced in patients with CVD who discontinue smoking. One of the earlier studies observed a 50% reduction in mortality caused by atherosclerotic disease within 5 years of cessation of smoking in both men and women [8]. A systematic review of 20 studies revealed a 36% crude relative risk reduction of mortality of patients with coronary heart diseases (CHD) who quit smoking when compared with those who continued the same, with most of the risk reduction realized within 2 years of cessation [5]. In comparison, the figures for the other secondary prevention strategies for CHD include: statin use—29% reduction, aspirin—15%, beta blockers—23%, angiotensin-converting enzyme inhibitors—23% [5]. The pooled relative risk for nonfatal reinfarction was 0.68 (95% confidence interval [CI]: 0.57–0.82) as reported in this systematic review. This effect of smoking cessation in CVD mortality has been observed in both sexes as well as in all ethnicities [9,10]. The reduction in all-cause mortality has been observed across all ages and is higher in those who discontinue smoking early [11] (Fig. 1).

The effect of smoking cessation in patients with left ventricular (LV) systolic dysfunction has been analyzed in a few studies. Data from the SOLVD (Studies of Left Ventricular Dysfunction) study was available for comparison of all-cause mortality rates between current smokers and never and ex-smokers (stopped smoking >2 years). Never smokers or ex-smokers, compared with current smokers, had a 30% reduced risk of dying over 41 months. Patients who had stopped smoking (>2 years) had comparable mortality rates with never smokers. The increased risk in smokers was accounted for by higher event rates in patients with ischemic LV dysfunction (n = 4,080 patients); the subgroup with nonischemic LV dysfunction (n = 1,428 patients) did not demonstrate this difference [12]. A previous analysis of more than 350,000 subjects screened for the MRFIT (Multiple Risk Factor Intervention Trial), followed up for idiopathic dilated cardiomyopathy deaths (n = 206), revealed a 39% higher risk for same in people smoking at least 1 pack of cigarettes per day versus never smokers and ex-smokers ($p < 0.001$) after adjustment for other CVD risk factors [13].

Smoking was found to increase the risk of sudden cardiac death (SCD) in patients with CVD [14], as well as in those without CVD [15]. Smokers were found to have a higher risk of appropriate implantable cardioverter-defibrillator shocks as well [16,17]. In another study, nicotine was found to result in a catecholamine-excess state, thereby predisposing subjects to life-threatening arrhythmias [18]. Smoking cessation was associated with significant reduction in deaths due to arrhythmias during

Table 1. Tobacco smoking and mortality

Cause of death	Never smokers	Ex-smokers	Quitters		Light smokers		Reducers		Heavy smokers	
			Cigarettes	Other type(s) of tobacco	Cigarettes	Other type(s) of tobacco	Cigarettes	Other type(s) of tobacco	Cigarettes	Other type(s) of tobacco
All-cause mortality										
Men	22.0	25.1	30.2	40.8	33.9	32.1	42.4	41.8	39.4	42.0
Women	15.0	14.7	20.1	21.1	21.4	22.6	32.8	32.6	28.3	31.7
Cardiovascular diseases										
Men	7.4	8.5	11.4	11.2	10.5	10.0	13.5	13.4	11.3	11.3
Women	4.9	3.8	5.8	2.4	5.4	2.5	6.3	0	6.3	11.1

Age-adjusted mortality rates (per 1,000 person-years) by smoking status, tobacco type, and sex, for deaths from all causes and cardiovascular diseases in the pooled study population (N = 19,732), Copenhagen Centre for Prospective Population Studies, Denmark, 1978–2000. Adapted, with permission, from Godtfredsen et al. [7].

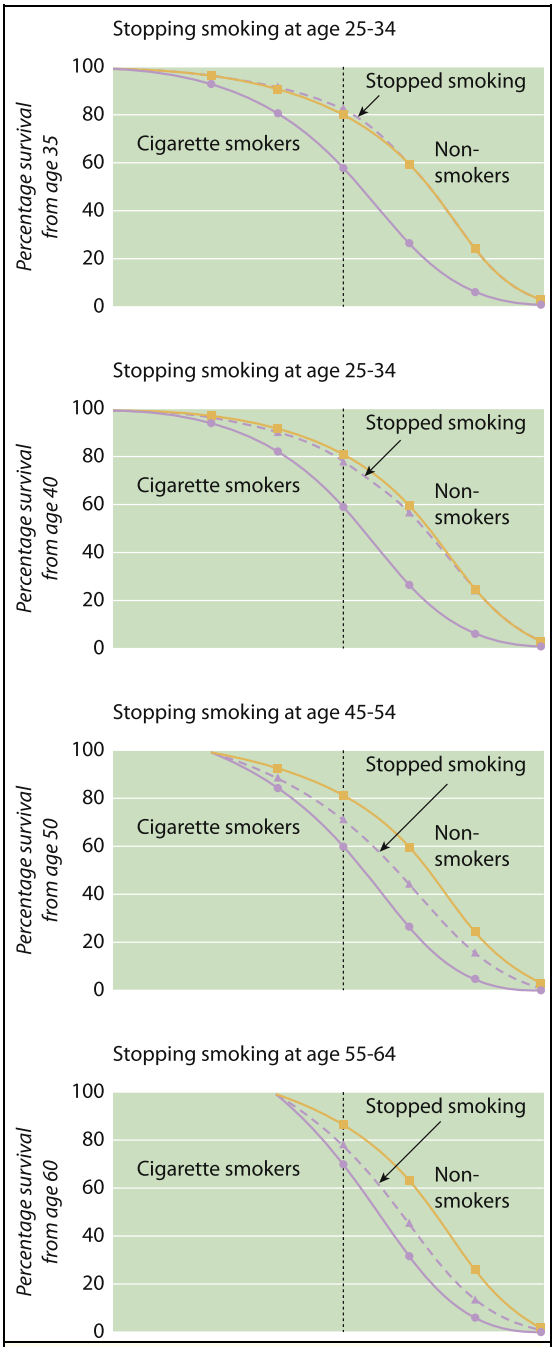

Figure 1. Effects on survival of stopping smoking cigarettes from ages 25–34 years (effect from age 35), ages 35–44 years (effect from age 40), ages 45–54 years (effect from age 50), and ages 55–64 years (effect from age 60). Reprinted with permission, from Doll [11].

prospective evaluation in a high-risk cohort of patients with post-MI LV dysfunction in the CAST (Cardiac Arrhythmia Suppression Trial) [19]. Occurrence of SCD in patients with a history of aborted SCD was higher in smokers than in those who quit smoking in a 4-year follow-up study [20]. Patients with coronary artery disease who quit smoking were found to have the same risk of SCD as never smokers with coronary artery disease [14].

Patients with coronary artery disease who have undergone revascularization have better long-term outcomes after smoking cessation. In the North American CASS (Coronary Artery Surgery Study) Registry, for patients who smoked at baseline and were randomized to bypass surgery, the 10-year survival was better for those who quit smoking after surgery (84%) versus 68% for those who continued to smoke ($p = 0.018$) [21]. Another study conducted at the Mayo Clinic (Rochester, Minnesota) demonstrated that the risk of mortality (relative risk [RR] = 1.76) and that of development of Q-wave MI (RR = 2.08) were higher in smokers than in quitters after percutaneous coronary intervention [22].

Smoking and hypertension. The effect of tobacco smoking and its cessation on blood pressure is a matter of debate. Smoking acutely increases blood pressure as well as heart rate due to sympathetic nervous system activity [23]. However, some studies reported lower blood pressure levels for habitual smokers than for nonsmokers [24], with an inverse relationship of blood pressure with serum levels of cotinine (a metabolite of nicotine, which has vasodilatory properties) [25]. In the Women's Health Study conducted in the United States, a cohort of 28,236 health professionals, who were free of hypertension, CVD, or cancer to begin with, were followed beginning in 1993, and it was found that current smoking ($\geqslant$15 cigarettes per day) was found to be modestly associated with development of hypertension (age adjusted hazard ratio: 1.11, 95% CI: 1.03–1.21) when compared with never smokers at the end of 9.8 years [26].

The effects of smoking cessation on blood pressure are by and large inconclusive, with some studies reporting an increase in blood pressure [27], and others reporting no increase [28,29] or even early reduction in blood pressure on cessation [30–32]. Various postulates including weight gain as a result of higher total food intake and increased stress as a consequence of smoking cessation are provided as reasons for the observed increase in blood pressure after tobacco cessation. However, smoking increases the risk of CVD and renal dysfunction in patients with hypertension [33].

Smoking, peripheral arterial disease, and abdominal aortic aneurysm. Smoking is an independent risk factor for development and progression of peripheral arterial disease (PAD) and

GLOBAL HEART, VOL. 7, NO. 2, 2012
July 2012: 129–138

claudication, with a dose-dependent effect found in cohort studies. The risk, which is there for both the sexes, may persist even after discontinuation of the habit [34]. In another analysis from the Women's Health Study, after a median follow-up of 12.7 years, the age-adjusted rate of PAD was more than 10-fold higher in smokers (>15 cigarettes per day) than in nonsmokers, with the risk being higher in pre-menopausal women. Though the risk of developing symptomatic PAD was substantially reduced on cessation of smoking, the risk remained higher than for nonsmokers even if the cessation was 20 years prior [35].

Smoking is the strongest risk factor for abdominal aortic aneurysm (AAA), with the risk being correlated stronger with the duration of smoking than with the number of cigarettes smoked per day [36]. The risk for AAA persists for as much as 10 years after cessation of smoking [37]. In patients with a small AAA, smoking cessation resulted in a relative risk reduction for elective AAA repair by 9% and for rupture by 38% over 10 years of follow-up [38].

Smoking and lipid abnormalities. Heavy smokers were observed to have higher levels of serum triglycerides, lower levels of serum high-density lipoprotein cholesterol [39,40], and higher serum levels of oxidized low-density lipoprotein (LDL), which promotes atherosclerosis [41]. These changes were observed to be reversed by 1–2 months after smoking cessation with the maximum reduction observed for LDL cholesterol, which reduced by a mean of 5.6% [42].

Maternal smoking and risk of congenital heart disease. Very few epidemiological studies have assessed the association of congenital heart diseases with maternal smoking. A Swedish population-based, case–control study showed an increased risk of atrial septal defects in infants of mothers who smoked (odds ratio [OR]: 1.63, 95% CI: 1.04–2.57) versus nonsmoking mothers [43]. In the Baltimore–Washington Infant Study—the first population-based case–control study of congenital heart diseases in the United States, self-reported first-trimester maternal cigarette consumption was associated with increased risk of certain types of congenital heart defects: secundum-type atrial septal defects (OR: 1.36, 95% CI: 1.04–1.78); right ventricular outflow tract defects (OR: 1.32, 95% CI: 1.06–1.65); pulmonary valve stenosis (OR: 1.35, 95% CI: 1.05–1.74); truncus arteriosus (OR: 1.90, 95% CI: 1.04–3.45); and levo-transposition of the great arteries (OR: 1.79, 95% CI: 1.04–3.10) [44]. In the National Birth Defects Prevention Study, maternal smoking during the month prior to pregnancy and in the first trimester was associated with an increased risk of septal defects [45].

Smoking and stroke. In a meta-analysis of 32 studies, the overall RR of stroke associated with cigarette smoking was estimated to be 1.5 (95% CI: 1.4–1.6) with subarachnoid hemorrhage demonstrating the highest RR of 2.9, cerebral infarction having an RR of 1.9, and cerebral hemorrhage being not associated (RR: 0.7) [46]. The risk of stroke was observed to be reduced by 2 years of abstinence in the Framingham cohort and was found to reach the levels of never smokers by 5 years [47,48].

Smokeless tobacco and CVD. The U.S. Food and Drug Administration has defined "smokeless tobacco" (ST) as any finely cut, ground, powdered, or leaf tobacco that is intended to be placed in the oral cavity. It also includes snuff. Current users of ST have a modest, but independent risk association with CVD mortality. The INTERHEART Study has shown that chewing tobacco alone was associated with an OR of 2.23 (95% CI: 1.41–3.52), and smokers who also chewed tobacco had the highest increase in risk (OR: 4.09, 95% CI: 2.98–5.61) [3]. A meta-analysis of 11 studies, mainly from the United States and Sweden yielded a RR of 1.13 (95% CI: 1.06–1.21) for fatal MI among current users versus nontobacco users. RR of fatal stroke was found to be 1.40 (95% CI: 1.28–1.54) [49]. Because of its sodium content and the presence of nicotine and licorice, ST use is associated with higher systolic and diastolic blood pressure. A study that compared the prevalence of hypertension in exclusive ST users versus nonusers in North India revealed significantly higher estimates for diastolic hypertension in exclusive ST users (40.9% versus 22.9%, p value = 0.01) [50]. The effects of various pharmacotherapy and behavioral therapy measures in assisting ST cessation were found to be inconclusive [51].

Smoking cessation and timeframe of cardiovascular benefits. The effects of smoking cessation on the cardiovascular system can be considered as a biphasic response, with an early improvement in dynamic components involving the vasoactive properties of the blood vessels, endothelial function, and vessel wall stiffness over the initial few months, which is followed by changes in atherosclerotic processes over the subsequent years. These are reflected on the clinical parameters as well as the CVD risk of the individual (Fig. 2).

The effects on blood pressure and arterial wall compliance were observed early after abstinence with significant reduction in blood pressure as early as 2 months [30] and reduction in the stiffness of vessel wall by 6 months [31]. The cardiovascular biomarkers including total leukocyte count, cholesterol levels, and urinary excretion of catecholamines were found to be significantly reduced in patients initiated on tobacco reduction/cessation therapy when compared with smokers as early as 3 months into therapy [42,52]. The plasma fibrinogen levels were significantly reduced in quitters when compared with smokers by 6 months [53]. Regions with antitobacco laws have noted reductions in hospital admission rates of MI as early as 3–6 months after enforcement of the ban [54]. Most of the risk reduction for mortality occurs in the first 1–3 years of cessation of smoking. The risk of nonfatal CVD was found to reduce by one-half within a year of cessation [10]. Most of the studies found that the risk of coronary events approach the level of nonsmokers by 3–5 years after cessation of smoking [55–57]. Similar results were observed in women as well [58,59]. However, many studies have concluded that the risk of CVD for quitters equals that for never smokers after 10 years of abstinence [58]. The risk for PAD persisted even 20 years after cessation [35].

TOBACCO CESSATION STRATEGIES

Tobacco cessation strategies can be community-/population-oriented and those targeting the individual. Community approaches include improving the awareness of the ill effects of smoking through campaigns and advertisements and including it in the educational curriculum of schools and colleges. Imposing a smoking ban in public spaces and increasing taxation for tobacco, banning tobacco advertisements, and inserting warning signs in tobacco products are other population-based strategies.

Approaches targeted at the individual include self-help, counseling, single pharmaceutical agents, combined pharmacotherapies, and pharmacotherapies combined with psychological counseling [1,60–62].

IMPACT OF VARIOUS TOBACCO CESSATION STRATEGIES ON CVD

Tobacco use results in tolerance and physical dependence, so withdrawal symptoms occur when the habit is discontinued. So interventions targeted at smoking cessation address both the physiological and psychological aspects of nicotine dependence. Analyses have documented the efficacy of both psychological counseling and pharmacotherapy in this regard [1].

Psychosocial interventions including behavioral therapy, telephone support, and self-help methods have been found to increase the quit rates, with more intense and sustained methods showing better results. Quitlines are telephone-based tobacco cessation services that help smokers quit through a variety of services, including counseling, providing information about treatment modalities, and

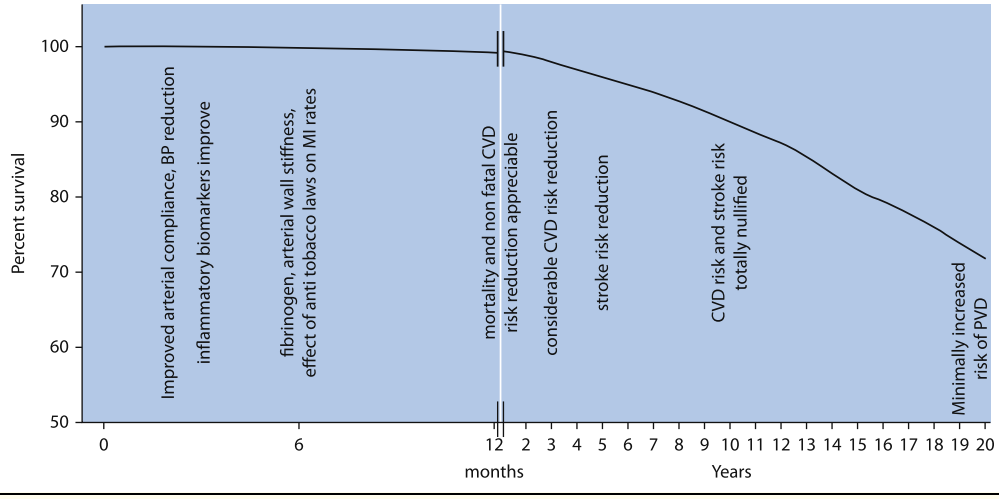

Figure 2. Timeline of benefits on smoking cessation pertaining to CVD risk. The curve indicates 20-year survival for men on cessation of smoking by 40 years of age. See text. BP, blood pressure; CVD, cardiovascular disease; MI, myocardial infarction; PVD, peripheral vascular disease.

GLOBAL HEART, VOL. 7, NO. 2, 2012
July 2012: 129–138

self-help materials. Quitline services can be tailored to the individual tobacco user based on the user's experience, tobacco use behavior, and motivations.

Such measures were found to be most effective when initiated after an episode of acute coronary syndrome in the hospital by a trained nurse [61]. However, such methods were not found to be much effective over a longer period of time. A meta-analysis of 16 randomized clinical trials (conducted in Europe, the United States, Canada, and Australia), each with a minimum follow-up of 6 months noted that brief interventions in CHD patients with no follow-up contact within 1 month had dismal quit rates at 6–12 months (OR: 0.92, 95% CI: 0.70–1.22). Whereas the quit rates improved with follow-up contacts after 1 month (OR: 1.98, 95% CI: 1.49–2.65), and it was estimated that about 10 CHD patients had to be treated with sustained interventions for 1 patient to remain abstinent from tobacco at the end of 1 year [60]. Hence, the guidelines for smoking cessation recommend the addition of pharmacotherapy to the counseling methods [61].

Pharmacotherapy. Nicotine replacement therapy (NRT) delivers a steady dose of nicotine to the system by alternate routes (noninhalational). All modes of NRT—transdermal patch, gum, inhaler, lozenges, and nasal spray—were found to be almost similarly effective, increasing the quit rates to nearly 2-fold over placebo [62]. Several studies have evaluated the safety of NRT use in patients with CVD, especially transdermal nicotine patch in both clinical and population-based settings. There was no increase in the event rate of MI and other endpoints in the active treatment group (transdermal patch) versus the placebo group [63]. A population-based case–control study (case subjects—smokers with first MI, control subjects—smokers without MI) observed no association between nicotine transdermal patch use and the risk of MI [64].

Studies assessing the direct impact of NRT on CVD risk reduction are not available and are rather impractical due to the need for large numbers and long follow-up. One study assessing the efficacy of high-dose nicotine patches reported a less-than-expected MI rate (expected MI rate was calculated from the data of Framingham study) over the study period of 1 year [65]. The acute effects of transdermal nicotine patch (increase in heart rate, increase in mean arterial pressure) are not observed in habituated smokers who are tolerant to vasoactive properties of lower doses of nicotine [63]. However, the smoking cessation guidelines recommend caution on the use of NRT in patients with an acute coronary event in the past 2 weeks or in those with a history of serious arrhythmias [1].

Bupropion is an antidepressant agent and is recommended by the guidelines as a first-line therapy for smoking cessation [61]. Systematic reviews have observed that bupropion is almost twice as effective as placebo for smoking cessation [66]. Bupropion with the nicotine patch doubled the rate of abstinence from smoking at the end of 1 year when compared with the nicotine patch alone in another study [67]. Bupropion is safe for use in smokers with stable CVD and was not found to result in adverse cardiac events in such patients [68]. However, bupropion appears to be less effective for smoking cessation when initiated in the setting of hospitalization for acute coronary events. The 12-week smoking abstinence rate with bupropion was not significantly different from that with placebo, but there was a nonsignificant higher adverse cardiovascular event rate in the bupropion group [69].

Nicotine receptor partial agonists such as varenicline or cytisine are also found to be effective in smoking cessation strategies. Compared with placebo, varenicline demonstrated superiority in smoking cessation (duration of therapy: 6 months, pooled risk ratio = 2.3) and to bupropion (duration of therapy: 12 months, pooled risk ratio = 1.52) with reported 6-month abstinence rates up to 33% [70]. However, there are concerns regarding the risk of adverse cardiovascular events in smokers using varenicline [71]. But a recent meta-analysis published in May 2012 that included 22 trials published to date, focused on events occurring during drug exposure, and analyzed findings using 4 summary estimates found no significant increase in cardiovascular serious adverse events associated with varenicline use [72].

Overall, various smoking cessation strategies targeting the individual smoker (behavioral and pharmacotherapy) result in low long-term quit rates (<30%) in patients with CVD [68], implying the need for combining the individual-based approaches with community-based strategies.

Effects of limiting SHS exposure. Unlike the case with lung cancer, SHS has a nonlinear dose response relationship with CVD, with excess risk even at lower doses [73]. Nonsmokers exposed to SHS were found to have blood markers suggesting inflammatory activity including total leukocyte count, raised C-reactive protein, fibrinogen, homocysteine, and oxidized LDL cholesterol levels, similar to the levels

observed in active smokers [74,75]. In a study assessing the acute effects of passive smoking, SHS exposure of 30-min duration provoked coronary vasoreactivity, the magnitude of which was higher in nonsmokers than in smokers [76]. Anginal thresholds are reduced on exposure to SHS.

The first results of a community-level smoking ban in Helena, Montana, USA, observed as much as a 40% reduction in hospital admission of patients with MI for the 6-month period during which the ban was in force when compared with the previous 6-month period. Once the ban was lifted, the hospital admission rates of patients with MI returned to baseline levels after 6 months [77]. In a meta-analysis of 11 studies in 10 locations, community smoking bans were found to be associated with an overall 17% risk reduction of MI [78]. The benefit of a smoking ban on MI rates was observed within as early as 3 months after the ban began [54]. The effects of smoking laws were found to accumulate over time as evidenced by a 15% risk reduction in MI rates at the end of the first year of a smoking ban to 36% by the end of a 3-year period [79].

Impact of smoking reduction. Reduction in the number of cigarettes smoked per day may result in clinically inconsequential improvement in blood parameters such as fibrinogen, leukocyte count, and blood cholesterol. However, these are not translated to improved CVD outcomes [7,68]. A prospective cohort study assessed the effect of smoking cessation and smoking reduction on the risk of MI and observed that whereas smoking cessation was beneficial, smoking reduction by as much as 50% failed to result in any clinical benefit [80].

Barriers to smoking cessation strategies. Smoking cessation approaches in developing countries are not organized. Even though population-oriented approaches, such as increasing taxation, ban of smoking in public places, banning adverts, are implemented with significant success, strategies targeted at the individual smoker have not been well evaluated to demonstrate success. For example, in India, there are only a few tobacco cessation clinics, and they are in tertiary care centers, which are inaccessible to the vast majority. Another problem is that in India, the tobacco cessation clinics are usually attached to a psychiatry department, hence the taboo and less acceptance. Patients often hesitate to attend psychiatry clinics due to the taboo of being labeled as a person having a psychiatric illness by societal peers. Hence, such services may not be received well by those who need it. It is sad that most of the academic or corporate hospitals in the developing world lack dedicated antitobacco clinics. There are hardly any self-help groups, and there are not many counselors.

One important reason for this phenomenon is that tobacco cessation strategies are not given adequate importance in the medical/nursing/paramedical curriculum. Lack of funds, lack of infrastructure, and physicians overburdened with clinical work add to the problem. Even though the patient will be most receptive (to advice regarding smoking cessation) following an admission for an acute coronary syndrome ("teachable moment"), the percentage of patients receiving advice regarding smoking cessation is very low [81,82]. It is found that a brief advice of 30 seconds by physicians produce quit rates of 5–10% per year [83]. But it is reported in a recent meta-analysis that offering assistance by physicians to quit smoking generated more quit attempts than those by providing advice alone [84].

Lack of training programs and the absence of successful models (smoking clinic) suitable for the developing world are other issues. Poverty and lack of awareness complicate these factors, impeding the success of such initiatives. The expense of pharmacotherapy is yet another factor. Nicotine patch and pharmacotherapy are often not affordable in a developing country setting: for example, a 28-tablet package of varenicline (1-mg strength) costs about INR 1,628 (approximately US$82) in India. In a qualitative study from Australia, the clients from disadvantaged sections desired to have financial incentives and access to free or subsidized NRT as part of a smoking cessation strategy [85]. But there are no studies comparing subsidized pharmacotherapy with other strategies.

Possible solutions. Because the lack of dedicated smoking treatment clinics is the crux of the issue, the priority should be to establish a few pilot centers in each country. Initially we have to test and modify such a facility to suit the local environment and then establish more of them.

The other key issue is the lack of follow-up of these patients. Because the penetration of mobile phones in most of the developing world is high, they can be used as an effective way for follow-up.

Including smoking cessation strategies in the medical curriculum is another strategy that can improve the situation. Physician associations in each country should realize the importance of the issue and should direct their members to adopt smoking cessation strategies.

GLOBAL HEART, VOL. 7, NO. 2, 2012
July 2012: 129–138

Future strategies. Development of new pharmacological agents that can reduce the dependence on nicotine is one option. Some of the drugs being tested include the newer generation neuronal nicotinic acetylcholine receptor partial agonists, cannabinoid receptor 1 antagonists, dopamine D3 antagonists, and monoamine oxidase inhibitors.

Nicotine vaccine is another modality that is being tested. Nicotine, being a small molecule, is rendered immunogenic by linking with a carrier protein, resulting in production of antibodies that bind to nicotine released into the bloodstream during smoking. This prevents nicotine from crossing the blood–brain barrier. With reduced amounts of nicotine reaching the brain, fewer stimulants are released and the pleasurable, positive-reinforcing effects of nicotine are diminished, thereby making it easier to quit smoking. NicVAX, the vaccine developed by GlaxoSmithKline (Brentford, United Kingdom) is in phase 3 development. The other nicotine-derived therapeutic vaccines are Nic-002, TA-Nic, and Niccine, being developed by Cytos Biotechnology/Novartis Pharmaceuticals (Zurich, Switzerland/Basel, Switzerland), Celtic Pharma (New York, New York, USA), and Independent Pharmaceutica (Stockholm, Sweden), respectively [86].

Strategies based on genomics can be used in tobacco cessation. Genetic testing has been proposed as a means to increase smoking cessation rates and thus improve smoking reduction approaches. Pharmacogenetics can be used to determine the potential effectiveness of antitobacco drugs. But it is felt that although genetics offers increasing opportunities to tailor drug treatment, and may in some cases provide useful risk prediction, other methods of personalizing care are likely to yield greater benefit to populations experiencing health disparities related to tobacco use [87].

CONCLUSIONS

Tobacco smoking is a major risk factor for atherosclerotic vascular diseases and smoking cessation remains the single most important secondary prevention strategy. Among the different tobacco cessation strategies available, psychosocial interventions coupled with pharmacological measures may result in good short-term results, but the overall long-term adherence is dismal. Many factors contribute to the failure of these strategies especially in the developing world where CVD is rampant. The benefits of avoidance of tobacco and cessation of tobacco use calls for global escalation of the antitobacco drive. Increasing the awareness about tobacco cessation strategies among the physician and paramedical community and establishment of tobacco cessation clinics will be helpful to some extent. It would be worthwhile to emphasize that mere reduction in the degree of smoking will not minimize the risk.

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